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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/824,787	04/04/2001	Maurice Zauderer	1821.0040001/EKS/TJS	2970

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EXAMINER
HARRIS, ALANA M

ART UNIT	PAPER NUMBER
1642	25

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/824,787	Applicant(s) ZAUDERER ET AL.	
	Examiner Alana M. Harris, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2003 and 06 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-46,81,83,84,119,121-123,158 and 160-166* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application (PTO-152)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .	6) ☐ Other:

Continuation of Disposition of Claims: Claims pending in the application are 38-51,53,54,56-66,68,69,74-78,80-89,91,92,94-104,106,107,112-116,118-128,130,131,133-143,145,146,151-155 and 157-209.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 47-51,53,54,56-66,68,69,74-78,80-82,85-89,91,92,94-104,106,107,112-116,118,120,124-128,130,131,133-143,151-155,157,159 and 167-209.

DETAILED ACTION

1. The first action on the merits mailed February 10, 2003 has been vacated. A new office action is presented below.

Election/Restrictions

2. Applicant's election without traverse of claims 38-46, 81, 83, 84, 119, 121-123, 158 and 160-166, which read on the elected species, nn. I-105 to V-113 of SEQ ID NO: 2 in Paper No. 21, received June 6, 2003 is acknowledged.

3. Claims 38-51, 53, 54, 56-66, 68-69, 74-78, 80-89, 91, 92, 94-104, 106, 107, 112-116, 118-128, 130, 131, 133-143, 145, 146, 151-155 and 157-209 are pending.

Claims 38-209 have been added.

Claims 1-37, 52, 55, 67, 70-73, 79, 90, 93, 105, 108-111, 117, 129, 132, 144, 147-150 and 156 have been canceled.

Claims 38, 84, 123 have been amended.

Claims 47-51, 53, 54, 56-66, 68, 69, 74-78, 80-82, 85-89, 91, 92, 94-104, 106, 107, 112-116, 118, 120, 124-128, 130, 131, 133-143, 151-155, 157, 159 and 167-209, drawn to non-elected inventions are withdrawn from examination.

Claims 38-46, 81, 83, 84, 119, 121-123, 158 and 160-166, which read on the elected species, nn. are examined on the merits.

Information Disclosure Statement

4. The information disclosure statement filed October 16, 2002 as Paper No. 15 was considered by the Examiner. A copy of paper no. 15 was mailed with the non-final rejection mailed February 10, 2003. However, copies of all documents "lined through" were not found in the file and were not considered by the Examiner. Applicant is invited to provide replacement copies.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 38-46, 81, 83, 84, 119, 121-123, 158 and 160-166 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 38-46, 81, 83, 84, 119, 121-123, 158 and 160-166 broadly claim an isolated polypeptide not more that 20-100 amino acids in length comprising at least one C35 peptide epitope defined as I-105 to V-113 of SEQ ID NO: 2, as well as a fusion polypeptide that comprises an isolated C35 peptide epitope defined as I-105 to V-113 of SEQ ID NO: 2 and a C35 peptide analog. The written description in this instant case only sets forth polypeptide, SEQ ID NO: 2 consisting of 115 amino acid residues and

including the defined epitope consisting of I-105 to V-113. The written description is not commensurate in scope with the claims drawn to arbitrary isolated polypeptides broadly defined by amino acid residue limitations, a fusion protein comprising the defined C35 peptide epitope and undefined amino acid sequences, as well as analogs, which encompass variant and mutated.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO: 2, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

At the time the application was filed Applicants only had possession of SEQ ID NO: 2 containing the amino acid epitope, I-105 to V-113 and not polypeptides that are analogs of SEQ ID NO:2 and fusion proteins. The fusion protein potentially contains at least 107 amino acids that have not been described. Likewise the polypeptide that comprises one C35 peptide epitope is surrounded by amino acids not described in the specification. The specification does not evidence the possession of all the possible variant and mutant polypeptides that could be or may not be capable of exhibiting activities of a wild type C35 polypeptide. There is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims do not meet the written description provision of 35 U.S.C. 112, first paragraph.

7. Claims 38-46, 81, 83, 84, 119, 121-123, 158 and 160-166 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 38-46, 81, 83, 84, 119, 121-123, 158 and 160-166 are broadly drawn isolated polypeptides not more that 20-100 amino acids in length comprising at least one C35 peptide epitope defined as I-105 to V-113 of SEQ ID NO: 2, as well as a fusion polypeptide that comprises an isolated C35 peptide epitope defined as I-105 to V-113 of SEQ ID NO: 2 and a C35 peptide analog. All of these broadly claimed polypeptides and fragments encompass variants which contain enumerable deletions and substitutions. The specification while being enabling for the polypeptide having the amino acid sequence of SEQ ID NO:2, does not reasonably provide enablement for variants that contain deletions, substations and mutations. There is no guidance as to how to make these divergent sequences. The products of these variant molecules may possess function that is not commensurate with the functions of the native protein. The variant amino acids may not maintain the activities proposed in the specification. It would seem that specific function(s) would be required to make the encoded protein useful for the applications disclosed in the specification, such as for treating breast and bladder carcinomas and in diagnostic applications. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar

activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of the ways in which the protein's structure relates to its function. The specification provides essentially no guidance as to which of the infinite possible choices is likely to be successful. The true fact of the state of the art in peptide chemistry is expressed succinctly in the accompanying Lazar article (Molecular and Cellular Biology 8(3): 1247-1252, March 1988). This article presents data that substantiates the fact that the introduction of mutations in an amino acid sequence will yield products with different biological activity from the wild type protein.

From the discussion above, it is clear that the predictability of changes to the amino acid sequence is practically nil as far as biological activities are concerned. The specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed amino acids in a manner reasonably correlated with the broad scope of the claims. Without such guidance, the changes which must be made in the nucleic sequence that encodes the variants of SEQ ID NO: 2, which results in limited sequence identity and/or undefined substitutions is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 160-164 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 160-162 are vague and indefinite in the recitation "peptide epitope analog". It is not clear how an analog is defined or how many amino acid residues encompass an analog. Accordingly, the metes and the bounds cannot be determined.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 38-46, 81, 122, 158, 160, 161, 163 and 166 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent application publication number US2002/0052308A1 (May 2, 2002). Sequence number 966 of U.S. Patent application publication # US2002/0052308A1 discloses an isolated polypeptide comprising a peptide epitope not more than 20 amino acids in length, see attached database sheet. The disclosed peptide, I-121 to V-129 is the same as the C35 peptide epitope, I-105 to V-113 of SEQ ID NO: 2. The disclosed peptide is regarded as C35 peptide epitope analog because it is identical to the claimed peptide. Also disclosed is a pharmaceutical

composition comprising the disclosed peptide epitope, see page 208, sections 0258-0260.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 38-46, 81, 83, 84, 119, 121, 122, 158 and 160-166 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent application publication number US2002/0052308A1 (May 2, 2002). U.S. Patent application publication number US2002/0052308A1 (May 2, 2002) teaches the C35 peptide epitope, I-105 to V-113 of SEQ ID NO: 2. The patent application publication does not teach the specific amino acid resides, I-105 to V113 comprised within a fusion protein and a pharmaceutically acceptable carrier.

However, the patent application publication does teach that "...polypeptides of the present invention, and immunogenic and/or antigenic epitope fragments thereof can be fused to other polypeptide sequences", see page 190, section 0112. It would have been *prima facie* obvious at the time of the claimed invention to compose a fusion protein with the specified fragment of SEQ ID NO: 2 in a pharmaceutical acceptable carrier because fusion proteins are useful in many applications. For instance, within a pharmaceutically acceptable carrier, the polypeptide of the present invention can be fused to marker sequences and a second protein in order to facilitate purification of the

fused polypeptide and as an antigenic tag, see page 191, sections 0114 and 0118 and page 208, sections 0258-0260. One of ordinary skill in the art would have been motivated by the teachings in the patent application publication because fusion proteins may also be engineered to improve characteristic of the polypeptide "[f]or instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification...", see bridging paragraph (section 0121) of pages 191 and 192.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ALANA HARRIS
PATENT EXAMINER

Alana M. Harris, Ph.D.
August 25, 2003